

Application No. 10/561,144
Amendment dated January 28, 2009
After Final Office Action of August 5, 2008

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REMARKS

In response to the previous Office Action, a non-final rejection (mailed on 9/19/2007), Applicants filed a response and amendment received on 4/17/2008. Said amendment canceled claims 16, 17, 29, 30, 39, 40, 43, 44 and amended claim 31, and added claims 52-54. In this Amendment, claims 55 and 56 have been added. Thus, claims 32, 32, 52-54 and 55-56 are at issue and present for examination.

It is noted by the Examiner that claims 1-15, 18-28, 33-38, 41, 42 and 45-51 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention in the previous Office Action, a non-final rejection (mailed on 9/19/2007).

No new matter has been added by this amendment.

Applicants respectfully reserve the right to pursue any non-elected, canceled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

It is submitted that the claims, herewith and as originally presented were in full compliance with the requirements of 35 U.S.C. § 112. The amendment of the claims, as presented herein, is not made for purposes of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, this amendment is made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendment should not give rise to any estoppel.

Reconsideration and withdrawal of the rejections of this application in view of the amendments and remarks herewith, is respectfully requested, as the application is in condition for allowance.

Applicant now turns to comments made by the Examiner in this Office Action as follows.

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OFFICE ACTION

1. Claims 31, 32 and 52-54 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner states, "Claims 31, 32 and 52-54 recite the phrase, '80% or more to the amino acid sequence starting at amino acid No. 1 in the amino acid sequence shown by SEQ ID NO: 2 or 4,' which is unclear and indefinite. It is unclear because whether the phrase is limiting the reference sequence to amino acids 1-104 of SEQ ID NO: 2 and amino acids 1-101 of SEQ ID NO: 4, or if the phrase is limiting the reference sequence to any amino acid sequence which starts at amino acid No. 1 of SEQ ID NO: 2 or 4. If their intended reference sequence is the entire sequence from amino acids 1-104 of SEQ ID NO:2 and the entire amino acid sequence from amino acids 1-101 of SEQ ID NO:4, it is suggested that the phrase be amended to recite, for example, '—identity of 80% or more to amino acids 1-104 of SEQ ID NO:2, or to amino acids 1-101 of SEQ ID NO:4—. In the interest of advancing prosecution, the noted phrase is interpreted to encompass any amino acid sequence which has 80% or more sequence homology to SEQ ID NO: 2 or 4, wherein said amino acid sequence starts at amino acid No. 1 of SEQ ID NO: 2 or 4.

Claims 31, 32 and 52-54 recite the phrase, "SEQ ID NO: 2 or 4, or a salt thereof, into contact," which is unclear and indefinite. It is unclear whether the phrase "salt thereof" refers to the protein being brought in contact with the receptor, or if refers to the polypeptides of SEQ ID NO:2 or 4. It appears that Applicants could fix this by amending the claim to recite "bringing a protein, or a salt thereof, comprising an amino acid..." In the interest of advancing prosecution, the noted phrase is interpreted as "bringing a protein, or a salt thereof, comprising an amino acid..."

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 31, 32, 52 and 54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, because the specification, while being enabling for SEQ ID NO: 2 and 4, does not reasonably provide enablement for any screening method for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality, which comprises bringing a protein or any salt thereof comprising *an amino acid sequence including any fragment and any mutant* having a sequence identity of 80%, optionally 90%, or more to any amino acid sequence starting at Amino Acid No. 1 in the amino acid sequence shown by SEQ ID NO:2 or 4, into contact with its receptor in the presence or absence of a test substance, and selecting the test substance that changes the ability of said protein or *any salt thereof* to bind to said receptor as a candidate for a prophylactic/therapeutic substance for a disease associated with abnormal differentiation of skeletal muscle cell and/or metabolic abnormality as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 31 and 32. In response to this rejection, Applicants have amended claim 31, and added claims 52-54, and traverse the rejection as it applies to the newly amended claims.

Applicants argue that because of the size of the SS169 protein and known conserved amino acid substitution as stated above, claims 31 and 32 are no longer so broad as to encompass a method of using (1) any protein ~60% sequence homology to SE IDNO: 2 or 4, (2) any partial peptide, and (3) any salt thereof that may be free of said protein or said partial peptide. A skilled artisan could produce an SS169 variant that had a homology of 80% or more to the amino acid sequence of SEQ ID NO:2 or 4 and retained physiological activities of SS169 (e.g., suppression of sugar uptake of a skeletal muscle cell upon insulin stimulation, suppression of glycogen synthesis in a skeletal muscle cell and the like) without undue experimentation based on the description of the specification as well as relatively high identity to the amino acid sequence of SEQ ID NO:2 or 4, and known conserved amino acid substitutions. The resulting SS169 variants are able to serve as a useful tool for the development of prophylactic/therapeutic drugs for diseases associated with sugar/lipid metabolic abnormalities as described in the specification, for example, page 84, line 9 to page 85, line 20. Further, Applicants allege that claims that encompass a protein having a homology of 80% or more in some applications have been

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allowed by the U.S. Patent & Trademark Office, e.g., USP 5,756,671 and USP 6,015,692, in spite of lack of working examples of any variants.

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. The scope of the claimed methods are so broad as to encompass any screening method for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality, which comprises bringing a protein or any salt thereof comprising *an amino acid sequence including any fragment and any mutant* having a sequence identity of 80%, optionally 90%, or more to any amino acid sequence starting at Amino Acid No. 1 in the amino acid sequence shown by SEQ ID NO:2 or 4, into contact with its receptor in the presence or absence of a test substance, and selecting the test substance that changes the ability of said protein or *any salt thereof* to bind to said receptor as a candidate for a prophylactic/therapeutic substance for a disease associated with abnormal differentiation of skeletal muscle cell and/or metabolic abnormality. Contrary to Applicants' argument, even in light of the fact that methods of making conservative substitutions were known in the art, claims are not limited to methods of using those amino acid sequences having 80% identity to SEQ ID NO: 2 or 4, wherein all other non-homologous residues are conservative substitutions. Instead, the claims are drawn to methods of using *an amino acid sequence including any fragment and any mutant* having a sequence identity of 80%, optionally 90%, or more to any amino acid sequence starting at Amino Acid No. 1 in the amino acid sequence shown by SEQ ID NO:2 or 4. In addition, although amino acids 1-104 of SEQ ID NO: 2 and amino acids 1-101 of SEQ ID NO:4 are 104 and 101 residues long, respectively, a polypeptide that has 80% identity to the reference sequences recited will comprise a sequence having up to ~21 modifications (alternatively ~11 modifications for 90%). For example, the genus of variants of SEQ ID NO:2 having 80% sequence identity to amino acids 1-104 of SEQ ID NO: 2 is $104! \times 19^{21} / (104-21)! / 21!$, is a total of 3.65×10^{48} variants. In light of the notion that, proteins having very different structures can have the same function (Kisselev et al, 2002), while proteins having very similar structure can have different activities (Witkowski et al, 1999; Wishart et al, 1995), one of skill in the art would not have been able to make and use the claimed invention without further guidance because the disclosure of the specification does not commensurate with the scope of the claimed invention. More importantly, claimed methods encompass any methods using *any salt thereof*, which means that one of skill in the art has to obtain any protein salt, i.e., protein crystals, as well

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as any salt that may associate with the protein such as NaCl to carry out the claimed methods. Although one of skill in the art would understand carrying out such methods in a solution, or in an aqueous environment, one would not be able to envision carrying out such methods using said crystals in solid state. Even if one were to carry out such methods in solid state, it requires methods of making protein crystals, which are highly unpredictable. Therefore, it would require undue experimentation for one skilled in the art to practice the claimed methods because the disclosure of the specification is limited to a single representative species of a protein having the amino acid sequence of SEQ ID NO: 2 or 4 that can be used by the claimed method. Further, Applicants' argument that USPTO has previously allowed "80% homology" language in USP 5,756,671 and USP 6,015,692, is not deemed persuasive because the instant application has been examined according to the current guidelines set forth by the USPTO and the MPEP. It is also noted that each application is examined on its own merits and any discussion in regard to the prosecution of other patent applications would be improper herein since it will require a detailed review of the record in each case. For the reasons provided herein and in the previous office action, the rejection under this statute is maintained.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a protein comprising *an amino acid sequence including any fragment and any mutant* having an identity of 80%, optionally 90%, or more to the amino acid sequence starting at Amino Acid No. 1 in the amino acid sequence shown by SEQ ID NO:2 or 4, or *any salt thereof* used in the claimed methods having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988)."

Applicants have amended claim 31 to limit the protein, or salt thereof, to the exact sequences of SEQ ID NO: 2 or 4, thereby negating the broader scope of including proteins with 80% identity or higher which could include fragments and mutants. Applicants respectfully request reconsideration.

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2. Claims 31, 32 and 52-54 are rejected under 35 U.S.C. § 102(b) as being anticipated by Lanctot et al. (US Patent Application Publication, US 2003/0125258, published Jul. 3, 2003).

The Examiner states, "The instant claims are drawn to a screening method for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality, which comprises bringing a protein comprising an amino acid sequence having an identity of 80%, optionally 90%, or more to the amino acid sequence starting at Amino Acid No. 1 in the amino acid sequence shown by SEQ ID NO:2 or 4, or a salt thereof, into contact with its receptor in the presence or absence of a test substance, and selecting the test substance that changes the ability of said protein or a salt thereof to bind to said receptor as a candidate for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality.

The rejection was stated in the previous office action as it applied to previous claims 31 and 32. In response to this rejection, Applicants have amended claim 31, and added claims 52-54, and traverse the rejection as it applies to the newly amended claims.

Applicants argue that Claim 31 is directed to a **screening method** for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality, which comprises bringing a protein comprising an amino acid sequence having an identity of 80% or more to the amino acid sequence starting at Amino Acid No. 1 in the amino acid sequence shown by SEQ ID NO:2 or 4, or a salt thereof, into contact with its receptor in the presence or absence of a test substance, and selecting the test substance that changes the ability of said protein or salt thereof to bind to said receptor as a candidate for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality. Applicants further argue that Lanctot et al. neither teach nor suggest the screening method of the instant invention which comprises the steps of selecting a test substance that changes the ability of SS196 or salt thereof to bind to its receptor as a candidate of a prophylactic/therapeutic agent for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality. Further, Applicants allege that Lanctot et al. did not disclose that BP-1, which is identical to SS169 of the present invention, is involved in the regulation of differentiation of skeletal muscle cell and/or metabolic abnormality.

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Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. In the instant case, the active steps of the methods taught by Lanctot et al. are no different from those of Applicants' claimed methods. Further, while the limitation regarding "prophylactic/therapeutic substance" is in reference to the compound that modifies the binding activity of the protein to the receptor, the claim does not recite any active step wherein one selects a compound having the recited functional limitations from any other substances that modulate the binding activity of the protein to the receptor. In fact, the claim states at the end that any compound that changes the binding activity of the protein to the receptor is a candidate for a "prophylactic/therapeutic substance." As such, the methods taught by Lanctot et al. meet the limitations of the claims because the test compound of Lanctot et al. is a candidate for a prophylactic/therapeutic substance according to the last part of the claim. The reference of Lanctot et al. specifically teaches a screening method comprising contacting BP-1 proteins, with a receptor in the presence of a molecule that may modulate binding of BP-1 proteins to a receptor (see paragraph [0144] under "x) Screening Methods Using BP-1 Products"). Further, as previously noted, the secreted human BP-1 protein taught by Lanctot et al. is identical to Applicants' SEQ ID NO: 2 (See SCORE, 20070817_151735_us-10-561-144-2.rag). Therefore, Lanctot et al. anticipate the claimed invention for the reasons provided herein and in the previous office action."

Applicants respectfully disagree. It is axiomatic that for a cited document to constitute an anticipation, all of the material elements of a claim must be found in the cited document. See, e.g., *In re Marshall*, 198 USPQ 344 (CCPA 1978); and *In re Kalm*, 154 USPQ 10 (CCPA 1967). Lanctot et al. does not meet this requirement. Claim 31 of the present application specifically refers to the limitation of "a disease associated with abnormal differentiation of skeletal muscle cell and/or metabolic abnormality". Lanctot et al. does not mention, refer to, or make any citation to "a disease associated with abnormal differentiation of skeletal muscle cell and/or metabolic abnormality". Therefore, Lanctot cannot anticipate claim 31. Applicants respectfully request reconsideration.

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CONCLUSION

In view of the remarks made herein, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. Please charge any required fee or credit any overpayment to Deposit Account No. 04-1105, 64656(46590).

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Respectfully submitted,

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